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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/506,535

07/05/2005

David Michael Evans

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EXAMINER

CHANG, CELIA C

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

07/17/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/506,535	Applicant(s) EVANS, DAVID MICHAEL	
	Examiner Celia Chang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 9-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-8 and 12 in the reply filed on May 7, 2008 is acknowledged. The traversal is on the grounds that the Greisbacher et al. reference is not published prior to the application date. This is not found persuasive because the Greisbacher et al. reference is a 102(f) reference which is "evidence" that another was in possession of the claims. Please note that the elected compound is an acid addition salt not FE999026.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8, 12 are prosecuted. Claims 9-11 are withdrawn from consideration per 37 CFR 1.142(b).

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(f) he did not himself invent the subject matter sought to be patented.

Claims 1-8, 12 are rejected under 35 U.S.C. 102(f) as being anticipated by Greisbacher et al. of record.

Please note that the Greisbacher et al. disclosed compounds encompassed by the claims with a "different" inventive entity. According to MPEP2137, applicants are required to provide a satisfactory showing by way of affidavit under 37 CFR 1.132 that the inventorship of the application is correct in that the reference disclosed subject matter invented by the applicant and the publication derived the subject matter from the applicant. In re Katz 215 USPQ 14.

3. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what structure is the term "R1 and R2 together are an o-xylene group optionally substituted on the aromatic ring...."

Please note that there is insufficient description on page 3 as to how this moiety is bonded to the structure. Clarification is required.

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4. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is drawn to pharmaceutical composition without a dosage limitation. Since pharmaceutical composition can neither be ineffective nor toxic, the claim is self conflicting.

5. Claims 8 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The scope of the claims are drawn to pharmaceutical compositions comprising an effective amount of a compound of claim 1 for treatment of a disease condition for which over activity of plasma kallikrein is a causative factor. It is unclear which condition the over activity of plasma kallikrein is causative. Over activity of kallikrein, which can be too much (over production) or too little (over degradation) kallikrein, can result from many conditions (see Campbell, Baumann or Gupta) but not necessarily the etiology of the disorder. The kallikrein system is very complexed. No nexus can be found in the specification or the prior art that structurally similar compounds of claim 1 active in the in vitro inhibitory Ki is inexorably linked to any specific disorder or symptom. Therefore, it is unclear what is the "dosage" required by claim 12 and how the specification can guide one skilled in the art to such a dosage calculation.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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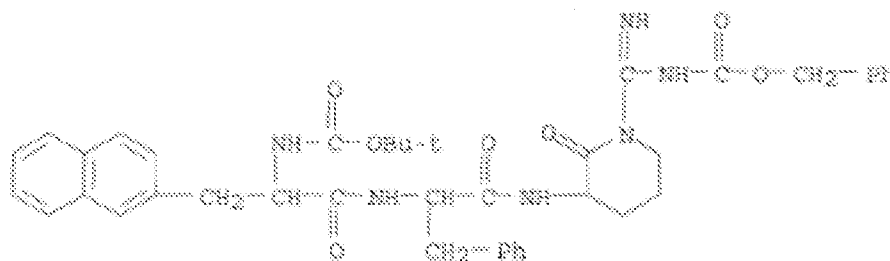
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over McIver et al. WO 93/08211 supplemented with CA119:226431 and CA 139:245221 (instant application), in view of Garrett et al. and Peake et al.

All references are analogous art in the field of compounds for biological activity by modifying the scissile bond.

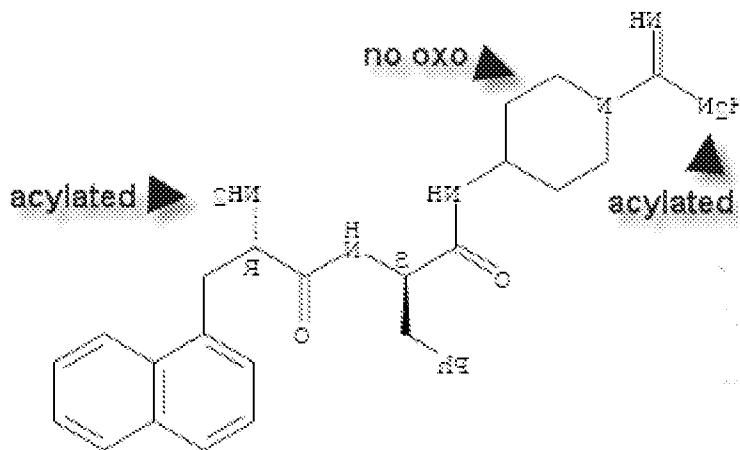
Determination of the scope and content of the prior art (MPEP §2141.01)

McIver et al. '211 disclosed structurally similar compounds for the instant activity in treating pain and inflammation. A particular species was structurally delineated by CA119:226431:



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the above species and a species of the claims as following:



Wherein the acylation at the base is prima facie obvious N-protection, and an oxo on the piperidine or not on the piperidine was taught by Garrett et al. and Peake et al. as equivalent moieties for such compounds. The Garrett et al. and Peake et al. references taught that cyclic

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argine (piperidine) or argine aldehydes (oxo-piperidine) are interchangeable units for such peptide mimics see Garrett et al. (p.61-62) and Peake et al. (p.455).

Finding of prima facie obviousness—rational and motivation (MPEP82142-2143)

One having ordinary skill in the art is deemed to be aware of all the pertinent art in the field. The particular species and the well recognized teaching of interchangeability between cyclic arginine and arginine aldehyde in the scissile peptide mimics would place the modification of the known compound of WO 93/08211 in possession of artisan in the field. The modification of a known compound using well recognized prima facie structural equivalency is prima facie obvious structurally.

In absence of unexpected results, the teaching, suggestion and motivation are well described in the prior art of record, thus, rendered the claims structurally prima facie. There is nothing unobvious in modification of a known compound using attributes well known in the field for such compounds.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
July 16, 2008

/Celia Chang/
Primary Examiner
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